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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,975	ABE ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14-38* is/are pending in the application.

4a) Of the above claim(s) *17-21,25-27,29-31,34-36 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14-16,22-24,28,32,33 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/14/2005 has been entered.

[2] Claims 1-12 and 14-38 are pending in the application.

[3] In view of applicants' request for continued examination, the amendment to the claims filed 1/21/2005 has been entered. This listing of the claims replaces all prior versions and listings of the claims.

[4] Applicants' arguments filed on 1/21/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[6] Newly submitted claims 1-2, 8, 11, and 37 are directed in part to an invention that is independent or distinct from the invention originally claimed for the following reasons.

In the instant amendment, the claims have been amended to recite "a protein coding sequence present in a Pir1, Pir2, Pir3, or Pir4 gene" and "protein coding sequence is present in a Pir1 or Pir2 gene." The specification states that GenBank Accession Number D13740 discloses a Pir1 gene sequence and GenBank Accession Number D13741 discloses a Pir2 gene sequence (pp. 28 and 36). The examiner can find no listing of an Accession Number for a Pir3 or Pir4 gene. A visual inspection of the polypeptide encoded by the Pir1 gene of GenBank Accession Number D13740 indicates that this amino acid sequence is the same as SEQ ID NO:1. Also, a visual inspection of the polypeptide encoded by the Pir2 gene of GenBank Accession Number D13741 indicates that this amino acid sequence is the same as SEQ ID NO:2. The examiner's interpretation is supported by applicants remarks at p. 12, top, of the instant response. In the election filed on 12/23/2003, applicants elected the invention of Group I, reciting the protein coding sequence of SEQ ID NO:1, without traverse. The sequences of SEQ ID NO:1 (encoded by a Pir1 gene) and SEQ ID NO:2 (encoded by a Pir2 gene) are distinct for those reasons set forth in the Office action mailed 7/3/2003 and, absent evidence to the contrary, the sequences of Pir3 and Pir4 are also distinct from the sequence of SEQ ID NO:1. As the sequences of a Pir1, Pir2, Pir3, and Pir4 gene are distinct, they necessarily require a separate sequence search.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 1-2, 8, 11, and 37 have been examined

only to the extent the claims read on the elected subject matter, i.e., a protein coding sequence of Pir1 encoding SEQ ID NO:1.

[7] Claims 17-21, 25-27, 29-31, 34-36, and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/23/2003.

Claim Objections

[8] The objection to claim 3 for reciting non-elected subject matter, i.e., SEQ ID NO:2, (¶ [9] of the Office action mailed 10/15/2004) is withdrawn in view of the amendment to the claim.

[9] The objection to claim 7 as being grammatically incorrect (¶ [10] of the Office action mailed 10/15/2004) is withdrawn in view of the amendment to the claim.

[10] Claims 1-2, 8, 11, and 37 are objected to as reciting non-elected subject matter. It is suggested that applicants amend the claims such that they no longer recite non-elected subject matter.

Claim Rejections - 35 USC § 112, Second Paragraph

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[11] The rejection of claims 1 (claims 5-6 rejected as being dependent therefrom), 2, 7, 8 (claims 9-10 and 32-33 rejected as being dependent therefrom), 11 (claims 12-13

and 28 rejected as being dependent therefrom), and 37 as being indefinite in the recitation of "a yeast Pir (protein internal repeat) cell wall protein coding sequence", "a Pir (protein internal repeat) motif coding sequence", or "a yeast cell wall protein coding sequence" (¶ [19] part [b] of the Office action mailed 10/15/2004) is withdrawn in view of the amendment to delete these terms from the claims.

[12] The rejection of claim 9 (claim 10 rejected as being dependent therefrom) as being confusing in the recitation of "expression cassette... comprising an expression vector" (¶ [19] part [c] of the Office action mailed 10/15/2004) is withdrawn in view of the amendment to the claim.

[13] The rejection of claims 13 and 22 (claim 23 rejected as being dependent therefrom) as being unclear in the recitation of "host cell... ...comprising a yeast cell wall" (claim 13) and "microorganism comprising a yeast cell wall" (¶ [19] part [d] of the Office action mailed 10/15/2004) is withdrawn in view of the amendment to the claims.

[14] Claims 1-12, 14-16, 22-24, 28, 32-33, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] The rejection of claim 1 (claims 2-7 dependent therefrom), 8 (claims 9-10 and 32-33 dependent therefrom), 11 (claims 12 and 28 dependent therefrom), 14 (claim 15 and 32-33 dependent therefrom), 16, 22 (claims 23-24 dependent therefrom), and 37 as being indefinite in the recitation of "a GAP promoter domain" is maintained for the reasons of record (¶ [19] part [a] of the Office action mailed 10/15/2004) and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue a skilled artisan would have recognized the meaning of the term at issue at the time of the invention, GAP promoters were known and used at the time of the invention, and provide an abstract (Sears et al.) in support thereof.

Applicants' argument is not found persuasive. There is no dispute that a GAP promoter was known and used by a skilled artisan in the art at the time of the invention as evidenced by Sears et al. (cited by applicants in the instant response). However, it remains unclear as to the scope of promoters that are meant to be encompassed by the term and those that are meant to be excluded. For example, is a GAP promoter meant to be limited to the GAP promoter sequence as used in the vectors of Sears et al.? Or is it meant to encompass additional GAP promoter sequences, including those that were not known at the time of the invention, e.g., the GAP promoter of Heo et al. (FEMS Yeast Res 4:175-184) and mutants and variants of known and unknown GAP promoters? Neither the specification nor the claims provide any defining characteristics of a "GAP promoter" that would allow a skilled artisan to distinguish those GAP promoter sequences that are meant to be encompassed by the term from those that are not. Consequently, the claims fail to define the metes and bounds of those GAP promoter sequences that are meant to be encompassed by the term. It is suggested that applicants clarify the meaning of the term "GAP promoter." If applicants maintain the position that the term was well-known to a skilled artisan, applicants are requested to elaborate on the meaning that would have been understood by a skilled artisan.

[b] Claims 1 (claim(s) 5-6 dependent therefrom) 2 (claim(s) 7 dependent therefrom), 8 (claim(s) 9-10 dependent therefrom), 11 (claim(s) 12 dependent therefrom), and 37 are indefinite in the recitation of "a protein coding sequence present in a Pir1...gene." While it is acknowledged that the specification provides an example (p. 27, top) of a Pir1 nucleic acid sequence and the encoded amino acid sequence, i.e., GenBank Accession Number D13740, it is unclear as to whether the term is meant to be limited to the protein coding sequence of GenBank Accession Number D13740 or whether GenBank Accession Number D13740 is merely an exemplary Pir1 and the term is meant to encompass additional Pir1 coding sequences. In this case, the specification fails to provide any identifying characteristics that would allow a skilled artisan to distinguish those Pir1-encoding sequences that are meant to be encompassed by the term from those that are not. Consequently, the claims fail to define the metes and bounds of those protein coding sequences present in a Pir1 gene that are meant to be encompassed by the claim. It is suggested that applicants clarify the meaning of the term.

It is noted that applicants argue that "[a] person of ordinary skill in the art reading Applicants' specification would have understood the meaning of a coding sequence that is present in a Pir1...gene." However, as neither the specification nor the claims define the meaning of the term, applicants are requested to elaborate on the meaning that would have been understood by one of skill in the art.

[c] Claims 3-4 are confusing in the recitation of "protein coding sequence comprises an amino acid sequence," "protein coding sequence comprises a protein," as coding

sequences, i.e., nucleic acid sequences, do not comprise proteins. In the interest of advancing prosecution, the terms have been interpreted as meaning that the protein coding sequence encodes an amino acid sequence or a protein. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[15] The written description rejection of claims 1-12, 14-16, 22-24, 28, 32-33, and 37 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and for the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the specification adequately describes a number of different enzymes, citing p. 17, lines 17-21 of the specification, argue the specification describes structural features of protein coding sequences present in a Pir1 gene, citing SEQ ID NO:1 and cites references that disclose Pir genes, citing pp. 16-17, and argue the term "GAP promoter" is art recognized and one can distinguish GAP promoters from others. Applicants argue that the specification adequately describes the claimed invention. Regarding essential and non-essential claimed subject matter, applicants assert they are unaware of case law establishing essentialness as a standard for determining written description compliance.

Applicants' argument is not found persuasive. Regarding the genus of enzyme coding sequences, as noted in a previous Office action, it is unclear to the examiner as to whether the enzyme coding sequence is an essential or non-essential element of the claimed invention. MPEP § 2163 states, "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." Thus, if the enzyme-coding sequence is an essential or critical feature of the claimed invention, then it should be adequately described in the specification. See also Example 18 of the Revised Interim Written Description Guidelines Training Materials, where a nucleic acid was not essential to the claimed invention. In this case, all working examples of the claimed invention are nucleic acids encoding fusion proteins comprising glycosyltransferases or proteases and it is unclear to the examiner as to whether a particular enzyme-coding sequence is essential to the claimed invention. Clarification is requested. Absent evidence to the contrary, the examiner has interpreted the enzyme-coding sequence as an essential or critical feature of the claimed invention.

Regarding the lack of written description, the Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." UC California v. Eli Lilly, (43 USPQ2d 1398). The CAFC in Eli Lilly further held that "[i]n claims to genetic material, however a generic

statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus." As noted in a previous Office action, with the recited genus of GAP promoter domains, protein coding sequences present in a Pir1 gene, or enzyme coding sequences, the recitation of "GAP promoter domain," "a protein coding sequence present in a Pir1...gene," or "an enzyme coding sequence" does not provide any structural information commonly possessed by members of the genus which distinguish the nucleic acid species within the genus from other nucleic acids such that one can visualize or recognize the identity of the members of the genus.

Also, for claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.,* structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means

that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification fails to disclose even a single representative species of a "GAP promoter domain" discloses only a single representative species of "a protein coding sequence present in a Pir1...gene," and discloses only three enzyme coding sequences that can be obtained by PCR amplification. In view of the lack of defining characteristics of "a GAP promoter domain," "a protein coding sequence present in a Pir1...gene," or "an enzyme coding sequence," the species encompassed by the genus are widely variant with respect to their structures. While one can argue that at least one representative species of each of these genera was known in the art at the time of the invention, MPEP § 2163 states "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." Further, it is noted that post-filed art discloses at least one GAP promoter sequence (Heo et al., FEMS Yeast Res 4:175-184) and it is unclear as to how one demonstrates possession of a genus of GAP promoter domains, when at least one species encompassed by the genus was not known at the time of the invention.

At least for the reasons stated above and the reasons of record, the specification fails to adequately describe the claimed invention.

[16] The scope of enablement rejection of claims 1-12, 14-16, 22-24, 28, 32-33, and 37 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and for the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue that a skilled artisan would have been able to make and use the full scope of the claimed invention using the guidance of the specification and further using standard cloning techniques without undue experimentation.

Applicants' argument is not found persuasive. The examiner maintains the position that, while the specification is enabling for a chimeric nucleic acid comprising a GAP promoter domain as taught by Sears et al. (cited by applicants in the instant response), a nucleic acid encoding the Pir1 of SEQ ID NO:1, and an enzyme coding sequence, undue experimentation is required to make the full scope of claimed chimeric nucleic acids for reasons that follow.

Breadth of the claims: The claims are so broad as to encompass a chimeric nucleic acid comprising: 1) any GAP promoter domain from any source, 2) any protein coding sequence that may be present in a Pir1 gene, including fragments thereof, and 3) any enzyme coding sequence. The dependent claims limit the Pir1 protein coding sequence and enzyme coding sequence. Regarding the recited GAP promoter domain, it is noted that the specification, other than identifying "GAP" as a promoter, fails to provide any defining characteristics of a "GAP promoter domain." Regarding the recited protein coding sequence, in construing the term in accordance with MPEP 2111, this coding sequence encompasses essentially any protein coding sequence. It is clear from the specification that the chimeric nucleic acids are meant to broadly encompass mutant and variant nucleic acids (see, e.g., pp. 13-14 and 16-17 and claim 4).

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: There is no dispute that at the time of the invention, at least one GAP promoter domain sequence was known in the art as evidenced by Sears et al. (cited by applicants in the instant response) and at least one Pir1 protein coding sequence was known in the art as evidenced by Akio et al. (cited in the IDS filed 6/10/2002). However, as noted above, the claims encompass variants and mutants of a known GAP promoter and a known Pir1 gene. The level of skill in the art was not so high at the time of the invention that a skilled artisan could predict a priori those variants of a known GAP promoter sequence or a known Pir1 gene sequence that would result in a functional promoter sequence or encode a functional protein having the desired activity/utility.

The amount of direction provided by the inventor; The existence of working examples: There is no dispute that the specification discloses specific working examples of a nucleic acid encoding a Pir protein fused to an enzyme coding sequence: Examples 1-9 as set forth at pages 27-34 of the instant specification. However, these working examples fail to provide the necessary guidance for making the full scope of claimed or recited chimeric nucleic acids, particularly as the specification fails to provide guidance for: isolating GAP promoter domains from other sources, altering known and unknown (those that are yet to be isolated) GAP promoter sequences with an expectation of maintaining promoter activity, for isolating other Pir1 coding sequences from other sources, altering known and unknown (those that are yet to be isolated) Pir1 coding sequences with an expectation of maintaining the desired activity/utility (see the

teachings of Branden et al., cited in the Office action mailed 2/24/2004, which supports the examiner's position).

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating variants of a promoter sequence and protein-encoding sequence were known in the art at the time of the invention, e.g., site-directed mutagenesis or hybridization, it was not routine in the art to screen for *all* GAP promoter sequences and polypeptide-encoding sequences having a substantial number of modifications, as encompassed by the instant claims. In view of the lack of guidance and working examples provided by the specification, one of skill in the art would have to resort to trial-and-error experimentation to make the full scope chimeric nucleic acids. Such experimentation was not routine at the time of the invention.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the experimentation required, it is clear that undue experimentation would have been necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[17] Upon further consideration, the rejection of claim(s) 1-2, 4, and 7 under 35 U.S.C. 102(b) as being anticipated by Moukadiri et al. (*J Bacteriol* 181:4741-4745; cited by applicants in the IDS filed May 06, 2002) is withdrawn. The examiner agrees with applicants' argument that the chimeric nucleic acid as taught by Moukadiri et al. does not comprise a GAP promoter domain.

[18] Upon further consideration, the rejection of claim(s) 1-2, 4-16, 22-24, 28, 32-33, and 37 under 35 U.S.C. 102(b) as being anticipated by Matilla et al. (*Glycobiol* 6:851-859; cited by applicants in the IDS filed June 10, 2002) as evidenced by Moukadiri et al. is withdrawn. The examiner agrees with applicants' argument that the chimeric nucleic acid as taught by Matilla et al. does not comprise a GAP promoter domain.

[19] Claim(s) 1-2, 4, 7-12, 16, 28, and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Klis et al. (WO 94/01567). The claims are drawn to a genus of

chimeric nucleic acids, expression cassettes, expression vectors, host cells, transformants and methods for producing a genus of immobilized proteins using said host cells or transformants. It is noted that the instant rejection has been made in view of the broad, but reasonable, interpretation of "a first domain comprising a protein coding sequence present in a Pir1...gene," which has been interpreted as meaning as few as two contiguous nucleotides from a Pir1 gene or two contiguous nucleotides encoding SEQ ID NO:1 (in claim 3). In other words, the first domain must comprise as few as two contiguous nucleotides of a Pir1 gene or two contiguous nucleotides of a nucleic acid encoding SEQ ID NO:1.

Klis et al. teach an expression vector comprising a chimeric nucleic acid encoding a C-terminal part of a protein that ensures anchoring in a yeast cell wall fused to an enzyme coding sequence for recombinant production of an enzyme "anchored" to the cell surface of a yeast (see pp 2-3). Klis et al. teach nucleic acid sequences encoding "anchor" proteins (pp. 31-69). These coding sequences comprise at least 2 contiguous nucleotides of a Pir1 gene or a nucleic acid encoding SEQ ID NO:1. Klis et al. teach the expression vector can comprise a GAPDH (synonymous with GAP) promoter (p. 24, Example 6). Klis et al. teach the use of their expression vector to transform yeast, including S. cerevisiae, and production of the encoded fusion protein, which is immobilized on the surface of the yeast cells (see pp. 9-26, Examples 1-10) and optionally collecting the yeast (p. 8, bottom). This anticipates claims 1-2, 4, 7-12, 16, 28, and 32-33 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[20] Upon further consideration, the rejection of claims 1-16, 22-24, 28, 32-33, and 37 under 35 U.S.C. 103(a) as being unpatentable over Matilla et al. in view of Moukadiri et al., Toh-e et al. (*Yeast* 9:481-489; cited by applicants in the IDS filed June 10, 2002), and Mrsa (*Yeast* 15:813-820; cited by applicants in the IDS filed June 10, 2002) is withdrawn. The rejection has not been withdrawn in view of applicants' arguments. Instead, the rejection is withdrawn in favor of the newly cited references of Klis et al. and Makarow et al. as noted below.

[21] Claim(s) 3, 5-6, 14-15, 22-24, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klis et al. in view of Makarow (WO 99/60152), Toh-e et al. (*Yeast* 9:481-489; cited by applicants in the IDS filed June 10, 2002), and Mrsa (*Yeast* 15:813-820; cited by applicants in the IDS filed June 10, 2002). The claims limit the protein coding sequence to SEQ ID NO:1 or a variant thereof with at least 80% identity to SEQ ID NO:1 or limit the enzyme coding sequence to encoding a glycosyltransferase.

Klis et al. disclose the teachings as described above. Klis et al. do not teach Pir1 (SEQ ID NO:1) as the yeast cell wall "anchor" protein encoded by their chimeric nucleic acid.

At the time of the invention, the use of at least one Pir protein, Pir4 or Hsp150, as an anchor protein for immobilizing proteins on a yeast cell surface was known in the art. For example, Makaorw (WO 99/60152) discloses the use of a chimeric nucleic acid encoding Hsp150 linked to a nucleic acid encoding alpha2,6-sialyltransferase (ST3N) for production of the encoded protein for yeast cell surface display of the encoded protein (pp. 2-3). Makarow teaches the use of the resulting yeast for sialylation of recombinant mammalian pharmaceutical proteins for decreasing the pharmaceutical protein's clearance rate (p. 1 and pp. 7-10). Makarow recognizes that fusion proteins comprising alpha-agglutinin as an anchor protein can be substituted by a fusion protein comprising Hsp150 as an anchor protein (p. 2, lines 19-22).

Mrsa et al. teach the equivalent characteristics of the four Pir proteins, i.e., Pir1, Pir2, Pir3, and Pir4, including covalent attachment to the cell wall of *S. cerevisiae* by a similar mechanism (page 813, right column, bottom to page 814, left column).

Toh-e et al. teach a nucleic acid sequence encoding a *Saccharomyces cerevisiae* Pir1 protein (page 483), represented by SEQ ID NO:1 (see sequence alignment attached to the Office action mailed 2/11/2004).

At the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Klis et al., Makarow, Mrsa et al., and Toh-e et al. to use Pir1 as an anchor protein in the vector of Klis et al. and ST3N as the enzyme. One

would have been motivated to replace the anchor protein of Klis with Pir1 because Pir1 is equivalent to the Pir4/Hsp150 protein as evidenced by Toh-e et al. and Mrsa et al. (see MPEP 2144.06 regarding art-recognized equivalence). One would have been motivated to replace the enzyme of Klis with ST3N because of the teachings of Makarow. One would have a reasonable expectation of success for replacing the anchor protein of Klis et al. with a Pir1-encoding sequence because of the results of Makarow, Toh-e et al., and Mrsa et al. One would have a reasonable expectation of success for replacing the enzyme of Klis et al. with ST3N because of the results of Makarow. Therefore, claims 3, 5-6, 14-15, 22-23, 24, and 37, drawn to the invention as described above, would have been obvious to one of ordinary skill in the art.

Conclusion

[22] Status of the claims:

- Claims 1-12 and 14-38 are pending.
- Claims 17-21, 25-27, 29-31, 34-36, and 38 are withdrawn from consideration.
- Claims 1-12, 14-16, 22-24, 28, 32-33, and 37 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Thursday and alternate Fridays from 6:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (571) 272-8300. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER